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Abstract

Dr. Robert Biggar of the National Cancer Institute (NCI), mainly focuses in his discussion on his research on AIDS, in particular his work in Denmark. He sets this in the larger context of the initial efforts of NCI and its director, Dr. Vincent DeVita, to deal with AIDS. He also describes NCI's first AIDS related conference, the reaction of scientists to AIDS, and the early efforts to investigate AIDS by the National Institute of Allergy and Infectious Diseases under its director, Dr. Richard Krause. He briefly describes his work before he joined the NIH. This is an interview with Dr. Robert Biggar of the National Cancer Institute (NCI) at the Executive Plaza North Building, Rockville, Maryland The interviewer is Dennis Rodrigues, program analyst, NIH Historical Office.

Rodrigues: Could you tell me about your professional background and training and how that prepared you for your involvement with AIDS?

Biggar: I lived overseas as a child in the Middle East during most of my growing up period. I went to college in California. I went to Baylor Medical School. I moved into pediatrics with the idea that I wanted a career in international health, particularly because of my early life experiences. I decided that the best way to get overseas was to become an epidemiologist, so I spent a couple of years with the Centers for Disease Control [CDC] studying epidemiology, supported by a fellowship in infectious diseases. From there I got a job with the NIH that took me to Ghana, West Africa. I studied Burkitt's lymphoma, a disease that is common among African children and is also associated with viruses. After four years in Ghana, I came back to the NIH in 1980. I finished up the analysis of the material that I brought back from Ghana. I was beginning to look for new projects in 1981, when the AIDS story began to break. AIDS seemed almost perfectly suited to my interests because, first, it had the components of a cancer, Kaposi's sarcoma, and, second, it had the aspects of being virally associated or at least potentially infectious disease-associated. From the very beginning, I suspected it was caused by a virus just by the nature of it. But the initial idea was that it was a cancer, perhaps infectious in origin. It certainly seemed a very interesting disease with which to be involved. My plate was fairly clean because I had just finished up the Ghana project material.

Rodrigues: How were things organized at NCI at that time? Was NCI attuned to what was happening in the field as far as looking for any new or unusual cancers? Were people going through the MMWR [Morbidity and Mortality Weekly Report] and taking note of anything that looked unusual, or were people aware of the possibility that something new might come along?

Biggar: I think that NCI involvement with AIDS resulted from the interest of individual investigators. There was no organized, formal surveillance of anything new coming up. People who became involved with AIDS at that stage were basically doing it on their own. They were working with what they gleaned from the literature themselves, heard in corridor rumors, and things of that type. I know of no organized surveillance; certainly, that had nothing to do with the way I heard about AIDS or my involvement in it. I became involved more or less by default, as did the others in my section.

Rodrigues: Did you begin working on AIDS independently or did you have collaborators at this point?

We are talking now about the summer of 1981. At that point I knew very little about the subject. I worked on it more or less by myself, trying to think of what I could do that would make a difference. I knew it was something that interested me, and I wanted to be involved in. But I had no access to the information, and there was no easy way to get involved. It was not that we were setting up a project. I had to think of a project, and then I had to sell it to the people who were responsible for funding what I did. They did not have a whole lot of interest in the subject. At that time, I was not sitting in the office that I am now. I was working under the direction of Dr. [Joseph] Fraumeni, who was the head of our section. Basically a solo operator, I did not really fit within the branch program as such, and I was not assigned to any section. This was fine when I was working on the Ghana data, because it did not make any sense for me to be working with anybody else. No one else knew the data. But as I got into a new project, it became less and less sensible for me to be on my own. About a year later, in 1982, I was transferred to working in this section, which at that time was called Family Studies, although we worked mostly with immunology and virology. My involvement with AIDS also had to do with the conference that was held by Dr. John Ziegler in September 1981, here at the NIH. I remember hearing the presentations at that conference and thinking to myself that this syndrome was going to be a major problem. That was really, if you will, what awakened my interest in AIDS. I was somewhat aware of AIDS; I did not specifically know much about it until I attended that conference. When I decided to become involved, I developed my own projects. At the same time, I became aware that there were other people within my branch, not necessarily working with me, who were also interested in the subject. One of them was my colleague [Dr.] James J. Goedert who is next door. He was, at that time, a new staff fellow at the NIH. He had seen one of these AIDS cases when he was an oncology fellow at Georgetown [University], and he was aware of it even before the announcement was made at the CDC [Centers for Disease Control]. Therefore, when he came to the NIH as a staff fellow, he thought that AIDS would be an interesting project in which to become involved. There was nobody at the top saying, "You have to be involved with this," or "You should get interested in this." Everybody followed his or her own interests, with the top brass saying, "If you are interested, sure go ahead, choose your own projects."

Rodrigues: You mentioned John Ziegler. He was the one who set up the conference. What role did he play? Where was he organizationally?

Biggar: Organizationally, he was also at the National Cancer Institute and actually had a background that was extremely similar to my own in many ways, although he is a good deal more senior than I am. He was, I think, the associate director of the Clinical Oncology Program. John had also spent many years in Africa studying Burkitt's lymphoma and had a great interest in AIDS because of this connection—Kaposi's sarcoma was part of the AIDS epidemic profile. We did not call it AIDS then, but we certainly were calling it a lump entity, a syndrome. Kaposi's was a major part of this syndrome. Ziegler had seen a lot of Kaposi's in Africa, and that was another thing that stirred his interest. He convened a conference of people both from the Public Health Service—the CDC and the NIH--and from the outside academic communities. This included most of the major actors in the field at that time. A number of clinicians came down from New York and discussed what they had seen, including Dr. A. [Alvin] E. Friedman-Kien. Dr. Mike [Michael] Gottlieb came in from Los Angeles. It was not a large conference. There were, I would guess, maybe 150 people at most, maybe not even that many. Most of the presentations were by clinicians, who presented their material, and academicians pointed out some background information, such as, "Kaposi's has always been a rare disease primarily occurring in Jewish men and Mediterranean people." What the academics had to say was, frankly, not very relevant, but what the clinicians from New York, Los Angeles, and San Francisco said was riveting in terms of showing something new happening in the field. That conference was conceived by John [Ziegler] to awaken the NIH's interest in this problem. It certainly awakened my interest, and I think it awakened the interest of many other individual investigators as well. I never saw any senior people pick up the lead in this. I always felt that there was not much central direction as to who was going to take control of AIDS and how they were going to handle it f

Rodrigues: Several people have told us that they were not certain if AIDS was really going to stay around or whether this outbreak of Kaposi's might have been just a blip in the public health profile.

Biggar: Absolutely. There are many other examples of diseases that have come and gone. The NIH was never designed to respond to emergency conditions. This has not been our role in the past. There was no sense on anybody's part in saying that we ought to stop doing what we were doing and focus our attention on AIDS. In fact, if anything, there was a stout resistance to such an attitude, because strange disease events in the past, like swine flu and Legionnaire's disease, had come and gone. Nobody paid any attention. The attitude that one should not divert major programs away from important subjects in order to take care of a transient phenomenon added to the complacency of the people who were administering the NIH at the time. I can understand this by looking at it from the point of view of an NIH investigator. He or she has to spend a couple of years putting together a protocol, getting it cleared, and getting bed space assigned for the examination of patients. An investigator is not readily going to walk away from the bed space reserved two or three years in advance. They are going to fight for those beds. After all, this is their life's work. With hindsight, you can say that maybe some of the preAIDS research being done was not very important. On the other hand, when you are doing the research, you think it is important or you would not do it. In fact, I think investigators did fight for their beds and sometimes resented the competition that AIDS represented.

Rodrigues: Dr. Arthur Levine said something interesting on this point concerning Dr. [Vincent] DeVita. Apparently there had appeared to be an outbreak of Hodgkin's disease in Albany, [New York]. However, it turned out to be a statistical artifact. Even then many people were alarmed by this "epidemic outbreak," and there were calls for diverting resources to look at this "new" problem. Dr. Levine speculated that this event may have influenced NCI's decision on making a major commitment to AIDS.

Biggar: Sensitized those making it, at least. There are many stories of that type. You are probably familiar with the herpes epidemic and all the fanaticism about, "My God, herpes is going to take over the nation." In fact, it was a non-event. Yes, there was a herpes epidemic, but it was never of great public health importance. I think the NIH shied away from being influenced by what was regarded as transient phenomena and thought that those sorts of studies belonged at the CDC, where it was their task to fight bush fires. The NIH was there to control what makes fire burn, if you want to use another analogy. Forget whether there is a bush fire this place or that place. The NIH was interested in finding out much more about the basic nature of fire, as such, not about the place that was burning.

Rodrigues: There was also a lot of bad fish that came in from Nova Scotia.

Biggar: Yes. I think they regarded those fish, and rightly so, as the province of the CDC rather than the NIH. Many of these epidemics have come and gone without much involvement from the NIH. Legionnaire's disease is another one. You can cite many different epidemics that would be transient phenomena and the NIH did not believe, as I saw it at least, that it should divert many resources towards the idea, if you will, of fighting brush fires.

Rodrigues: In your view, when do you think that perception changed in the majority of people's minds? When did people finally say, "Wait a minute, AIDS is not a transient problem. This is something that is going to be with us; this is a large emerging problem?"

Biggar: I am not privy to the information circulating at the levels in which you are probably interested. The problem, as I saw it, was that there was a very severe lack of coordinated leadership at the top. I think that different people decided at different times that AIDS was going to be of some importance and interest. In the institute that I was with, the Cancer Institute, DeVita never wholeheartedly embraced the subject of AIDS. In fact, I think he really resented the intrusion that AIDS was making on his folks. When you think about it that is not an unreasonable position. DeVita's mandate was to study cancer. It was not to study infectious diseases. As it became more and more obvious that this was going to be an infectious disease problem, he became increasingly leery about going after the subject. He did not like the idea that some of his senior researchers were, in fact, diverting attention away from cancer, their primary mission as he saw it, into the subject of AIDS. That is my own feeling about it. You would have to talk to DeVita to get a clearer view of this. But, my belief was that when DeVita looked at [Dr. Robert] Gallo, whom you know, his thoughts were about whether Gallo should divert his attention away from what might be retrovirus-related cancers, i.e., HTLV-I [Human T-cell Leukemia Virus-type 1], and go after something that was purely an infectious disease. That was a major thing. Gallo was one of the stars, but suddenly Gallo is not doing much in the way of cancer research anymore. This must have bothered DeVita. The same thing with [Dr. Samuel] Broder. Broder was head of NCI's Developmental Oncology Program, when he suddenly switched focus and started trying to control retroviruses. I am sure DeVita felt upset about this idea. Broder was taking time and attention away from developing cancer chemotherapy. I do not think DeVita ever was sold on the idea that the Cancer Institute ought to be a focal point for AIDS research.

I know that in the case of NIAID, the administrator did a rather poor job of coordinating. Dick [Dr. Richard] Krause was the head of NIAID, and it is my opinion that he, in fact, was reluctant to get into the whole subject of AIDS. I know that, in 1982, he had Bob [Dr. Robert] Edelman coordinate some activities. At that point they were thinking about setting up a real AIDS activity area. I interviewed with them for a job and proposed that I might want to spend between \$100,000 and \$200,000 on investigating the subject. Krause felt this was simply too much. They did not have those kinds of resources available. Maybe that was an excuse for not wanting to hire me. I do not know, but I do know they did not hire anybody else, and they never really developed a program until Krause left and [Dr. Anthony] Fauci took over. What they had was very uncoordinated and was really not a centrally directed program at all. When Fauci took over, I think, their plans were obviously developed very fast. That is when you get the development of the MAC [Multi-Center AIDS Cohort] Studies and so forth.

Rodrigues: Getting back to administrative actions. The first clearly identifiable event relating to AIDS at NIH was that workshop in September 1981, in terms of an institute doing something in a formalized way.

Biggar: That is correct. That conference really was a presentation. There was nothing organized beyond that presentation to the best of my knowledge. It was basically John Ziegler saying to the NIH community: "Look, folks, I think this is going to be important, and you had better pay attention to it." But that was as far as it went. John quit the NIH soon after that. He did not have an opportunity to do anything about taking the lead. He went out to San Francisco. I think he threw the ball up in the air and said, "Somebody should catch this and go with it." But I never saw anybody catch it. Many individual investigators took the ball and scrambled their own different ways, but it was not a coordinated effort.

Rodrigues: One of the things I came across was the establishment of a working group to coordinate research efforts on Kaposi's sarcoma, and [Dr. Joseph] Fraumeni was involved.

Biggar: When was this?

Rodrigues: This was in mid-1982.

Biggar: Possibly. I will not deny it. I do not know anything about such a working group. I certainly was not involved in it.

Rodrigues: What I found curious was that the group was established, but there was no follow-up. There were no minutes. There was just one short paragraph saying, "We're going to establish this working group." It is kind of a mystery.

Biggar: I never knew about it. It certainly never played a role in my life. If there was such a working group trying to coordinate research, I do not think it was too effective. I did not even know it existed. That is not a surprise, I suppose. I do not know what they would do about Kaposi's. It was fairly obvious from the early days of AIDS that, although Kaposi's was part of this syndrome, it was really only one part, and the fundamental problem was not going to be a problem with cancer, but with immune suppression. That posed a difficulty for the NIH because there is no National Institute of Immune Suppression. There was an institute for cancer, but cancer was only part of AIDS. There was an institute for infectious diseases, but nobody knew for sure that AIDS was an infectious disease. Everybody had a good excuse for not saying, "Well, it's my province. I'm going to take it over." I mean, it was not anybody's particular mandate. That was a problem.

Rodrigues: Yes. I have often thought of the NIH as a landscape of established disease problems. When a new problem is dropped in, it bounces around.

Biggar: That is precisely right. I think that is a reasonable analogy to make. It was mainly the individual investigators who set about doing things on their own. Here is an anecdote about something that happened to me personally when I was an individual investigator. I was going over to Denmark. One of the ways I saw to investigate the AIDS problem was to get away from the epidemic, which was at that time in New York and the West Coast cities. I was trying to get to a gay community outside the United States, where they had just as many associated life-style risk factors to see if they had immune suppression in that community. This was my way of addressing whether or not the problem causing the disease was the nitrites, the gay behavior, or contact with the United States--was it really the evil beast in all of this? If AIDS was due to contact with the United States, then the disease had to be infectious. That was the way I saw it. In October 1981, partly by good chance, I was invited to go to Denmark. Initially, [Dr. Joseph] Fraumeni agreed that I could go to Denmark. Then President [Ronald] Reagan came along and imposed a freeze on all except essential spending on foreign travel. Fraumeni came back to me and said that my trip was not something that he could call essential. I had to pay for the trip myself, which is one of the things that came out in Randy Shilts's book. From an administrative point of view, AIDS was not regarded as an essential problem. When Reagan announced that all except essential foreign travel would be curtailed, I got cut. Even then I was not about to lose the opportunity, so I went anyway, without its being an NIH-funded trip. I thought that I had to get outside the United States to see what was going on. I had very few other ways to become involved in any AIDS projects. At that point, setting up a project by myself was not a very easy thing to do. I had to get some collaborators working in a place where I could find a problem.

Rodrigues: You mentioned that you worked at the CDC before coming to the NIH. Were you in contact with any of the epidemiologists at the CDC?

Biggar: I was there between 1973 and 1975. Some of the same people were still there. But now we are talking about 1981, six years later. The CDC turns over fairly rapidly--and I did not know any of the CDC principals working in the AIDS area. I did not know Jim [Dr. James] Curran. I know them now, but I did not know them then. I really was not in contact with them and only heard corridor discussion or presentations at meetings. I paid a lot of attention to what they said when they came up to the meeting that Ziegler had. I have always had a lot of respect for the CDC and think they have performed rather well under the circumstances. I think they have taken a lot of criticism, but I think they do a magnificent job.

Rodrigues: Were you involved in any way with the working group that was set up out of Building 1 and chaired by Bob [Dr. Robert] Gordon?

Biggar: I have not been involved in any of the working groups. I think I am probably at much too low a level for that kind of thing, which mostly involves the administrators. I did not know anybody who was involved. In fact, I do not know any front line AIDS researcher who is involved in those things. Such groups never played any practical role in what I did or in what any of the people I know did. As far as I know, they were simply there as a buffer between the various congressional interests in AIDS and public relations aspects of AIDS and the people who are actually doing the work, who like myself, are down in the trenches. I think they simply view their role as a buffer between the two. I do not know that they had any particular role to play in doing any of the research themselves.

Rodrigues: Thank you, Dr. Biggar.